

Docket No.: 06223.052 (12795\*3)  
(PATENT)

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Patent Application of:  
Jerry L. McLaughlin et al.

Docket No.: 06223.052

Application No.: 10/717746

Confirmation No.: 8781

Filed: November 20, 2003

Art Unit: 1615

For: CONTROL OF CANCER WITH  
ANNONACEOUS EXTRACTS

Examiner: Thurman K. Page

**INFORMATION DISCLOSURE STATEMENT (IDS)**

MS Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

Pursuant to 37 CFR § 1.97(b) and in order to comply with Applicant's duty of disclosure under 37 CFR § 1.56, the following and attached information is brought to the attention of the Examiner, especially the accompanying form PTO/SB/08 and the references listed therein. Attached is a copy of each cited reference if required under 37 CFR 1.98. It is requested that the references be expressly considered during the prosecution of this application, and that the references be made of record therein and appear among the "References Cited" on any patent to issue therefrom.

In accordance with 37 CFR § 1.97(h), the filing of this Information Disclosure Statement shall not be construed as an admission that the information cited is, or is considered to be, material to patentability as defined in 37 CFR § 1.56(b). In accordance with 37 CFR § 1.97(g), the filing of this Information Disclosure Statement shall not be construed to mean that a search has been made or that no other material information as defined in 37 CFR § 1.56(a) exists. It is submitted that the Information Disclosure Statement is in compliance with 37 CFR § 1.98.

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Because this Information Disclosure Statement is filed within three months of the filing date of a national application, within three months of date of entry of the national stage, before the mailing of a first Office action on the merits, or before the mailing of a first Office action after the filing of a request for continued examination, no fee is believed due. If any fees are due in connection with the filing of this response, including any fees that may be required under 37 CFR § 1.97(c), the Commissioner is authorized to charge such fees or credit any overpayment to Deposit Account No. 03-2775.

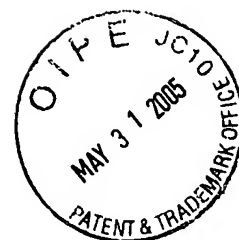
Respectfully submitted,  
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<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  <i>(Use as many sheets as necessary)</i>				Application Number	10/717746-Conf. #8781
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				Attorney Docket Number	12795-00003-US
Sheet	1	of	4		

U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. <sup>1</sup>	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code <sup>2</sup> (if known)			
	AA	4,855,319	08/08/89	Mikolajczak et al.	
	AB	5,229,419	07/20/93	McLaughlin et al.	
	AC	5,536,848	07/16/96	McLaughlin et al.	
	AD	5,717,113	02/10/98	McLaughlin et al.	
	AE	5,955,497	09/21/99	McLaughlin et al.	
	AF	6,242,483	06/05/01	McLaughlin et al.	

FOREIGN PATENT DOCUMENTS						
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		Country Code <sup>3</sup> -Number <sup>4</sup> -Kind Code <sup>5</sup> (if known)				

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NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
	CA	Ahammadsahib, K. I. et al., "Mode of Action of Bullatacin: A Potent Antitumor and Pesticidal Annonaceous Acetogenin", Life Sciences, Vol. 53, pp. 1113-1120 (1993).	
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	CC	Alali, F.Q. et al., "Annonaceous Acetogenins: Recent Progress", Journal of Natural Products, Vol. 62, No. 3, pp. 504-540 (1999).	
	CD	Alfonso, D. et al., "SARs Of Annonaceous Acetogenins In Rat Liver Mitochondria," Natural Toxins, Vol. 4, pp. 181-188, plus erratum p. 295 (1996).	
	CE	Avalos, J. et al., "Guinea Pig Maximization Test Of The Bark Extract From Pawpaw, <i>Asimina triloba</i> (Annonaceae)", Contact Dermatitis, Vol. 29, pp. 33-35 (1993).	
	CF	Ayre, S. G. et al., "Insulin, Chemotherapy, And The Mechanisms Of Malignancy: The Design And The Demise of Cancer", Medical Hypotheses, Vol. 55, No. 4, pp. 330-334 (2000).	
	CG	Caparros-Lefebvre, D. et al., "Possible Relation Of Atypical Parkinsonism In The French West Indies With Consumption Of Tropical Plants: A Case-Control Study", Lancet, Vol. 354, pp. 281-286 (1999).	
	CH	Cullen, J. K. et al., "Insulin-like Growth Factor Receptor Expression And Function In Human Breast Cancer", Cancer Research, Vol. 50, pp. 48-53 (1990).	
	CI	Fang, X.-P. et al., "Annonaceous Acetogenins: An Updated Review", Phytochemical Analysis, Vol. 4, pp. 27-48 (part 1) and pp. 49-67 (part 2), (1993).	
	CJ	Gu, Z.-M. et al., "Quantitative Evaluation Of Annonaceous Acetogenins In Monthly Samples Of Paw Paw ( <i>Asimina triloba</i> ) Twigs By Liquid Chromatography/Electrospray Ionization/Tandem Mass Spectrometry", Phytochemical Analysis, Vol. 10, pp. 32-38 (1999).	

Examiner Signature		Date Considered	
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Substitute for form 1449A/B/PTO  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (Use as many sheets as necessary)				<b>Complete if Known</b>	
				Application Number	10/717746-Conf. #8781
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Sheet	2	of	4	Attorney Docket Number	12795-00003-US

CK	Gu, Z.-M. et al., "Determining Absolute Configurations Of Stereocenters In Annonaceous Acetogenins Through Formaldehyde Acetal Derivatives And Mosher Ester Methodology", Journal of Organic Chemistry, Vol. 59, pp. 5162-5172 (1994).	
CL	Gu, Z. M. et al., "Annonaceous Acetogenins: Potent Mitochondrial Inhibitors With Diverse Applications", Recent Advances In Phytochemistry, Vol. 29, Plenum Press, New York, pp. 249-310 (1995).	
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CN	He, K. et al., "Three New Adjacent Bis-tetrahydrofuran Acetogenins With Four Hydroxyl Groups From <i>Asimina Triloba</i> ", Journal of Natural Products, Vol. 59, pp. 1029-1034 (1996).	
CO	He, K. et al., "Additional Bioactive Annonaceous Acetogenins From <i>Asimina Triloba</i> (Annonaceae)", Bioorganic and Medicinal Chemistry, Vol. 5, No. 3, pp. 501-506 (1997).	
CP	Hollingworth, R. M. et al., "New Inhibitors Of Complex I Of The Mitochondrial Electron Transport Chain With Activity As Pesticides", Biochemical Society Transactions, Vol. 22, pp. 230-233 (1994).	
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CT	Hui, Y.-H. et al., "Bullatacin And Bullatacinone: Two Highly Potent Bioactive Acetogenins from <i>Annona Bullata</i> ", Journal of Natural Products, Vol. 52, No. 3, pp. 463-477 (1989).	
CU	Johnson, H. A. et al., "Thwarting Resistance: Annonaceous Acetogenins As New Pesticidal And Antitumor Agents," in Biologically Active Natural Products: Pharmaceuticals, ACS Symposium Book, Las Vegas, Nevada, CRC Press, Boca Raton, pp. 173-183 (1999).	
CV	Landolt, J. L. et al., "Determination of Structure-Activity Relationships Of Annonaceous Acetogenins By Inhibition Of Oxygen Uptake In Rat Liver Mitochondria", Chemico-Biological Interactions, Vol. 98, pp. 1-13 (1995).	
CW	Lewis, M. A. et al., "Inhibition Of Respiration At Site I By Asimicin, An Insecticidal Acetogenin Of The Pawpaw, <i>Asimina Triloba</i> (Annonaceae)", Pesticide Biochemistry and Physiology, Vol. 45, pp. 15-23 (1993).	
CX	Martin, J. M. et al., "Chemical Defense In the Zebra Swallowtail Butterfly, <i>Eurytides Marcellus</i> , Involving Annonaceous Acetogenins", Journal of Natural Products, Vol. 62, pp. 2-4 (1999).	
CY	McLaughlin, J. L. et al., "Crown Gall Tumours In Potato Discs And Brine Shrimp Lethality: Two Simple Bioassays For Higher Plant Screening And Fractionation", in Methods in Plant Biochemistry, Vol. 6, Academic Press, London, pp. 1-31 (1991).	
CZ	McLaughlin, J. L. et al., "Simple (Bench-top) Bioassays And The Isolation Of New Chemically Diverse Antitumor And Pesticidal Agents From Higher Plants", Recent Advances In Phytochemistry, Vol. 33, Kluwer Academic/Plenum Publishers, New York, pp. 89-132 (1999).	
CA1	McLaughlin, J. L. et al., "Simple Bench-top Bioassays (Brine Shrimp And Potato Discs) For The Discovery Of Plant Antitumor Compounds: Review Of Recent Progress," book chapter in Human Medicinal Agents From Plants, ACS Symposium Series 534, American Chemical Society, Washington, D.C., pp. 112-137, (1993).	
CB1	McLaughlin, J. L. et al., "The Use Of Biological Assays To Evaluate Botanicals", Drug Information Journal, Vol. 32, No. 2, pp. 513-524 (1998).	
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Sheet	3	of	4	Attorney Docket Number	12795-00003-US

CD1	Miyoshi, H. et al., "Essential Structural Factors Of Annonaceous Acetogenins As Potent Inhibitors Of Mitochondrial Complex I", Biochimica et Biophysica Acta, Vol. 1365, pp. 443-452 (1998).
CE1	Morre, D. J. et al., "Mode Of Action Of Bullatacin, A Potent Antitumor Acetogenin: Inhibition Of NADH Oxidase Activity Of HELA and HL-60, But Not Liver, Plasma Membranes", Life Sciences, Vol. 56, No. 5, pp. 343-348 (1995).
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CG1	Oberlies, N. H. et al., "Annonaceous Acetogenins: Thwarting ATP Dependent Resistance" in New Trends and Methods in Natural Products Research, Proceedings of the 12th International Symposium on Plant Originated Crude Drugs, May 20-22, 1998, The Scientific and Technical Research Council of Turkey, Ankara, pp. 192-223 (1999).
CH1	Oberlies, N. H. et al., "Structure-Activity Relationships Of Diverse Annonaceous Acetogenins Against Multidrug Resistant Human Mammary Adenocarcinoma (MCF-7/adr) Cells", Journal of Medicinal Chemistry, Vol. 40, No. 13, pp. 2102-2106 (1997).
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CN1	Rieser, M. J. et al., "Determination Of Absolute Configuration Of Stereogenic Carbinol Centers In Annonaceous Acetogenins by <sup>1</sup> H- and <sup>19</sup> F- NMR Analysis of Mosher Ester Derivatives", Journal of the American Chemical Society, Vol. 114, No. 26, pp. 10203-10213 (1992).
CO1	Rupprecht, J. K. et al. "Asimicin, A New Cytotoxic And Pesticidal Acetogenin From The Paw Paw, <i>Asimina Triloba</i> (Annonaceae)", Heterocycles, Vol. 24, No. 5, pp. 1197-1201 (1986).
CP1	Rupprecht, J. K. et al., "Annonaceous Acetogenins: A Review", Journal of Natural Products, Vol. 53, No. 2, pp. 237-278 (1990).
CQ1	Satake, S. et al., "Up-Regulation Of Vascular Endothelial Growth Factor In Response To Glucose Deprivation", Biology of the Cell, Vol. 90, pp. 161-168 (1998).
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CS1	Shimada, H. et al., "Membrane Conformations And Their Relation To Cytotoxicity Of Asimicin And Its Analogues", Biochemistry, Vol. 37, No. 3, pp. 854-866 (1998).
CT1	Shimada, H. et al., "The Localisations In Liposomal Membranes Of The Tetrahydrofuran Ring Moieties Of The Annonaceous Acetogenins, Annonacin And Sylvaticin, As Determined By <sup>1</sup> H NMR Spectroscopy", Pharmacological Research, Vol. 37, No. 5, pp. 357-364 (1998).
CU1	Woo, M. H. et al., "Asitribolins A and B: Cytotoxic Mono-THF Annonaceous Acetogenins From The Seeds of <i>Asimina Triloba</i> ", Phytochemistry, 50, pp. 1033-1040 (1999).
CV1	Woo, M. H. et al., "Asimilobin and <i>Cis</i> - and <i>Trans</i> -muriolinones, Novel Bioactive Annonaceous Acetogenins From The Seeds of <i>Asimina Triloba</i> ", Journal of Natural Products,

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		Vol. 58, No. 10, pp. 1533-1542 (1995).	
	CW1	Woo, M. H. et al., "Asitribin and Asiminenins A and B, Novel Bioactive Annonaceous Acetogenins From The Seeds of <i>Asimina Triloba</i> ", <i>Heterocycles</i> , Vol. 41, No. 8, pp. 1731-1742 (1995).	
	CX1	Woo, M. H. et al., "16, 19-Cis-murisolin and murisolin A, Two Novel Bioactive Mono-tetrahydrofuran Annonaceous Acetogenins From <i>Asimina Triloba</i> Seeds", <i>Bioorganic and Medicinal Chemistry Letters</i> , Vol. 5, No. 11, pp. 1135-1140 (1995).	
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	CZ1	Ye, Q. et al., "Absolute Stereochemistries Of Giganin And Loganin, Bioactive Non-tetrahydrofuran Ring Annonaceous Acetogenins From <i>Asimina Longifolia</i> ", <i>Heterocycles</i> , Vol. 43, No. 8, pp. 1607-1612 (1996).	
	CA2	Zeng, L. et al., "Recent Advances In Annonaceous Acetogenins", <i>Natural Product Reports</i> , Vol. 13, pp. 275-306 (1996).	
	CB2	Zhao, G. -X. et al., "(2,4- <i>cis</i> )-Asimicinone and (2,4- <i>trans</i> )-Asimicinone: Two Novel Bioactive Ketolactone Acetogenins From <i>Asimina Triloba</i> (Annonaceae)", <i>Natural Toxins</i> , 4, pp. 128-134 (1996).	
	CC2	Zhao, G. -X. et al., "The Absolute Configuration Of Adjacent bis-THF Acetogenins and Asiminocin, A Novel Highly Potent Asimicin Isomer From <i>Asimina Triloba</i> ", <i>Bioorganic &amp; Medicinal Chemistry</i> , Vol. 4, No. 1, pp. 25-32 (1996).	
	CD2	Zhao, G. -X. et al., "The Absolute Configuration Of Trilobacin And Trilobin, A Novel Highly Potent Acetogenin From The Stem Bark Of <i>Asimina Triloba</i> (Annonaceae)", <i>Tetrahedron</i> , Vol. 51, No. 26, pp. 7149-7160 (1995).	
	CE2	Zhao, G. -X. et al., "Additional Bioactive Compounds And Trilobacin, A Novel Highly Cytotoxic Acetogenin, From The Bark Of <i>Asimina Triloba</i> ", <i>Journal of Natural Products</i> , Vol. 55, No. 3, pp. 347-356 (1992).	
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	CG2	Zhao, G. -X. et al., "Bullatin And Bullanin: Two Novel, Highly Cytotoxic Acetogenins From <i>Asimina Triloba</i> ", <i>Heterocycles</i> , Vol. 38, No. 8, pp. 1897-1908 (1994).	
	CH2	Zhao, G. -X. et al., "Biologically Active Acetogenins From Stem Bark Of <i>Asimina Triloba</i> ", <i>Phytochemistry</i> , Vol. 33, No. 5, pp. 1065-1073 (1993).	
	CI2	Morin, M. J., "From oncogene to drug: development of small molecule tyrosine kinase inhibitors as anti-tumor and anti-angiogenic agents", <i>Oncogene</i> , Vol. 19, pp. 6574-6583 (2000).	

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